

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>7</sup> : <b>C07K 14/00, C12P 21/06</b>		A2	(11) International Publication Number: <b>WO 00/61614</b> (43) International Publication Date: <b>19 October 2000 (19.10.00)</b>
(21) International Application Number: <b>PCT/US00/09534</b>			(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
(22) International Filing Date: <b>6 April 2000 (06.04.00)</b>			
(30) Priority Data: 60/128,701 9 April 1999 (09.04.99) US 60/142,821 8 July 1999 (08.07.99) US 60/149,448 18 August 1999 (18.08.99) US 60/164,751 12 November 1999 (12.11.99) US			
(71) Applicant (for all designated States except US): HUMAN GENOME SCIENCES, INC. [US/US]; 9410 Key West Avenue, Rockville, MD 20850 (US).			Published <i>With declaration under Article 17(2)(a); without abstract; title not checked by the International Searching Authority.</i>
(72) Inventors; and			
(75) Inventors/Applicants (for US only): RUBEN, Steven, M. [US/US]; 18528 Heritage Hills Drive, Olney, MD 20832 (US). NI, Jian [CN/US]; 5502 Manorfield Road, Rockville, MD 20853 (US). KOMATSOULIS, George [US/US]; 9518 Garwood Street, Silver Spring, MD 20901 (US). ROSEN, Craig, A. [US/US]; 22400 Rolling Hill Road, Laytonsville, MD 20882 (US). SOPPET, Daniel, R. [US/US]; 15050 Stillfield Place, Centreville, VA 22020 (US).			
(74) Agents: HOOVER, Kenley, K. et al.; Human Genome Sciences, Inc., 9410 Key West Avenue, Rockville, MD 20850 (US).			
(54) Title: UNCOUPLING PROTEINS			

*FOR THE PURPOSES OF INFORMATION ONLY*

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakhstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

***What Is Claimed Is:***

1. An isolated nucleic acid molecule comprising a polynucleotide selected from the group consisting of:
  - (a) the polynucleotide shown as SEQ ID NO:X or the polynucleotide encoded by a cDNA included in ATCC Deposit No:Z;
  - (b) a polynucleotide encoding a biologically active polypeptide fragment of SEQ ID NO:Y or a biologically active polypeptide fragment encoded by the cDNA sequence included in ATCC Deposit No:Z;
  - (c) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:Y or a polypeptide epitope encoded by the cDNA sequence included in ATCC Deposit No:Z;
  - (d) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(c), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A residues or of only T residues.
2. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide comprises a nucleotide sequence encoding a soluble polypeptide.
3. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide comprises a nucleotide sequence encoding the sequence identified as SEQ ID NO:Y or the polypeptide encoded by the cDNA sequence included in ATCC Deposit No:Z.

4. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide comprises the entire nucleotide sequence of SEQ ID NO:X or a cDNA included in ATCC Deposit No:Z..

5. The isolated nucleic acid molecule of claim 2, wherein the polynucleotide is DNA.

6. The isolated nucleic acid molecule of claim 3, wherein the polynucleotide is RNA.

7. A vector comprising the isolated nucleic acid molecule of claim 1.

8. A host cell comprising the vector of claim 7.

9. A recombinant host cell comprising the nucleic acid molecule of claim 1 operably linked to a heterologous regulating element which controls gene expression.

10. A method of producing a polypeptide comprising expressing the encoded polypeptide from the host cell of claim 9 and recovering said polypeptide.

11. An isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:  
(a) the polypeptide shown as SEQ ID NO:Y or the polypeptide encoded by the cDNA;

- (b) a polypeptide fragment of SEQ ID NO:Y or the polypeptide encoded by the cDNA;
- (c) a polypeptide epitope of SEQ ID NO:Y or the polypeptide encoded by the cDNA; and
- (d) a variant of SEQ ID NO:Y.

12. The isolated polypeptide of claim 11, comprising a polypeptide having SEQ ID NO:Y.

13. An isolated antibody that binds specifically to the isolated polypeptide of claim 11.

14. A recombinant host cell that expresses the isolated polypeptide of claim 11.

15. A method of making an isolated polypeptide comprising:  
(a) culturing the recombinant host cell of claim 14 under conditions such that said polypeptide is expressed; and  
(b) recovering said polypeptide.

16. The polypeptide produced by claim 15.

17. A method for preventing, treating, or ameliorating a medical condition, comprising administering to a mammalian subject a therapeutically effective amount of the polypeptide of claim 11 or the polynucleotide of claim 1.

18. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

(a) determining the presence or absence of a mutation in the polynucleotide of claim 1; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of said mutation.

19. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

(a) determining the presence or amount of expression of the polypeptide of claim 11 in a biological sample; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

20. A method for identifying a binding partner to the polypeptide of claim 11 comprising:

(a) contacting the polypeptide of claim 11 with a binding partner; and

(b) determining whether the binding partner effects an activity of the polypeptide.

21. A method of screening for molecules which modify activities of the polypeptide of claim 11 comprising:

(a) contacting said polypeptide with a compound suspected of having agonist or antagonist activity; and

(a) assaying for activity of said polypeptide.

<110> Human Genome Sciences, Inc.

<120> Uncoupling Proteins

<130> PT009PCT

<140> Unassigned  
<141> 2000-04-06

<150> 60/142,821  
<151> 1999-07-08

<150> 60/149,448  
<151> 1999-08-18

<150> 60/164,751  
<151> 1999-11-12

<150> 60/128,701  
<151> 1999-04-09

<160> 66

<170> PatentIn Ver. 2.0

<210> 1  
<211> 733  
<212> DNA  
<213> Homo sapiens

<400> 1	60
gggatccgga gcccaaatct tctgacaaaaa ctcacacatg cccaccgtgc ccagcacctg	120
aattcgaggg tgcaccgtca gtcttcctct tccccccaaa acccaaggac accctcatga	180
tctcccgac tcctgaggtc acatgcgtgg tgggtggacgt aagccacgaa gaccctgagg	240
tcaagttcaa ctggtagctg gacggcgtgg aggtgcataaa tgccaaagaca aagccggcggg	300
aggagcagta caacagcactg taccgtgtgg tcagcgtccct caccgtctg caccaggact	360
ggctgaatgg caaggagtag aagtgcagg tctccaacaa agccctccca acccccccateg	420
agaaaaccat ctccaaagcc aaagggcagc cccgagaacc acagggtgtac accctgcccc	480
catcccgaaa tgagctgacc aagaaccagg tcagcctgac ctgcctggc aaaggcttct	540
atccaaagcga catcggcgtg gagttggaga gcaatgggca gccggagaac aactacaaga	600
ccacgcctcc cgtgctggac tccgacggct ctttttccct ctacagcaag ctcaccgtgg	660
acaagagcag gtggcagcag gggAACgtct tctcatgctc cgtgatgcgt gaggctctgc	720
acaaccacta cacgcagaag agcctctccc tgcgtccggg taaatgagtgc gacggccgc	733
gactctagag gat	

<210> 2  
<211> 1560  
<212> DNA

&lt;213&gt; Homo sapiens

<400> 2		
ctagtgccgc tgcgagcgccg cgcggaccgc gcacaggcgg cggagccgg atggccgc	60	
ctggccctgg gcgcgcgcgc gcacgacac cagcttagag ccaggactga agcttcaaga	120	
tggctgacca ggaccctgccc ggcacatcgcc ccctccagca aatggtgcc tcaggcaccg	180	
gggctgtggt tacctctctc ttcatgacac ccctggacgt ggtgaagggtt cgcctgcagt	240	
ctcagcggcc ctccatggcc agcgagctga tgccttcctc cagactgtgg agcctctctc	300	
ataccaaatg gaagtgccctc ctgtattgca atggtgtccct ggagccctcg tacctgtgcc	360	
caaatggtgc cgcgtgtgcc acctggttc aagaccctac cgccttcaact ggcaccatgg	420	
atgccttcgt gaagatgtg aggcacgagg gcaccaggac cctctggagc ggcctccccc	480	
ccacccctggt gatgactgtg ccagctaccg ccatctactt cactgcctat gaccaactga	540	
aggccttcgt gttgtgtca gcccgtaccc ctgacccctta cgcacccatg gtggctggcg	600	
cgcgtggcccg cctggggacc gtgactgtga tcagccccc ggagctttag cggacaaagc	660	
tgcaggetca gcatgtgtcg taccgggagc tgggtgcctg tggctgaact gcagtggctc	720	
agggtggctg ggcgtcaactg tggctggctg gggggccccc tggcccttcga gatgtgcct	780	
tctcagccct gtactgggtc aactatgagc tggtaagag ctggctcaat gggctcaggc	840	
cgaaggacca gacttctgtg ggcgtaccc ttgtggctgg tggcatctca gggacgggtgg	900	
ctgcagtgtc gactctaccc ttgcgttgg taaagaccca acgcccaggc gctctgggag	960	
cgatggaggc tggagatgtg aacccttcgc atgtggactc cacctggctg ctgtgcgg	1020	
ggatccgggc cgagtcgggc accaaggac tctttgcagg cttcccttc cggatcatca	1080	
aggctggccc ctccctgtgcc atcatgtca gcacctatga gttcgccaaa agctcttcc	1140	
agaggctgaa ccaggacccg cttctggcg gctgaaaggg gcaaggaggc aaggaccccg	1200	
tctctccac ggtatggggag agggcaggag gagaccacca caagtgcctt ttccctcagca	1260	
ctgagggagg gggcttggc cccatccctc cccgcacaa gtcggggc aggctgtcc	1320	
ctctggccgg cccagactt cctcagacac aacttcttc tgcgtgcctca gtcgtgggaa	1380	
tcatcaactt cccacccccc aagtcaaga ccaaatcttc cagctgcccc cttcgtgttt	1440	
ccctgtgtt gctgttagtgc ggcgtgtc caggaaccaa gaaggccctca gcctgggtga	1500	
gtctccctga ccctgttaa ttcccttaatg ctaaagatga tgaaaaaaaaaaaaaaa	1560	

&lt;210&gt; 3

&lt;211&gt; 1566

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

<400> 3		
tgcacccacg cgtccgcggg cgcgtggcg gacgcgtggg tcgcggagcc gggccgcacc	60	
cgcgcgaccc tcttgataact gatggacatt gtgtggcca gaggcaggga tggttggcta	120	
tgaccccaaa ccagatggca ggaataacac caagttccag gtggcagtgg ctgggtctgt	180	
gtctggactt gttactcgcc cgtgtatcg tcccttcgac gtcatacaaga tccgtttcca	240	
gttcagcat gagcgcctgt ctgcgtatcg ccccagcgcgca aagtaccatg gcatcctcca	300	
ggcctctagg cagattctgc aggaggaggg tccgacagct ttctgaaag gacacgtccc	360	
agctcagatt ctctccatag gctatggagc tgcgttgcgc tgcgttgcgc aatgtgttgc	420	
ggagctggtc cacagaggca gctgttgcgc cgcggggaa ttctcgttgc accttgcgtatg	480	
ttgtggccctg gctgcctgtt tggccaccct cactgttgcac cccgtggatg ttctgcgcac	540	
ccgcttgcac gtcaggggtt agcccaaggt ctataatacg ctgcgcac gctgtggggac	600	
catgtatagg agcgaaggcc cccaggtttt ctacaaaggc ttggctccca ccttgcgtcgc	660	
catcttcccc tacgcggggc tgcgttgcgc ttgttgcgttgc acctgtacaa	720	
gtggccata ccagccgaag gaaagaaaaa tgagaacccctc caaaacccctc ttgtggcag	780	
tggagctgtt gtcatacgca agaccctgcgac atatccgcgtt gaccccttca agaaggcg	840	

<210> 20  
<211> 351  
<212> PRT  
<213> *Homo sapiens*

<400> 20  
 Met Ala Asp Gln Asp Pro Ala Gly Ile Ser Pro Leu Gln Gln Met Val  
 1 5 10 15  
 Ala Ser Gly Thr Gly Ala Val Val Thr Ser Leu Phe Met Thr Pro Leu  
 20 25 30  
 Asp Val Val Lys Val Arg Leu Gln Ser Gln Arg Pro Ser Met Ala Ser  
 35 40 45  
 Glu Leu Met Pro Ser Ser Arg Leu Trp Ser Leu Ser Tyr Thr Lys Trp  
 50 55 60  
 Lys Cys Leu Leu Tyr Cys Asn Gly Val Leu Glu Pro Leu Tyr Leu Cys  
 65 70 75 80  
 Pro Asn Gly Ala Arg Cys Ala Thr Trp Phe Gln Asp Pro Thr Arg Phe  
 85 90 95  
 Thr Gly Thr Met Asp Ala Phe Val Lys Ile Val Arg His Glu Gly Thr  
 100 105 110  
 Arg Thr Leu Trp Ser Gly Leu Pro Ala Thr Leu Val Met Thr Val Pro  
 115 120 125  
 Ala Thr Ala Ile Tyr Phe Thr Ala Tyr Asp Gln Leu Lys Ala Phe Leu  
 130 135 140  
 Cys Gly Arg Ala Leu Thr Ser Asp Leu Tyr Ala Pro Met Val Ala Glu

145	150	155	160
Ala Leu Ala Arg Leu Gly Thr Val Thr Val Ile Ser Pro Leu Glu Leu			
165	170	175	
Met Arg Thr Lys Leu Gln Ala Gln His Val Ser Tyr Arg Glu Leu Gly			
180	185	190	
Ala Cys Val Arg Thr Ala Val Ala Gln Gly Gly Trp Arg Ser Leu Trp			
195	200	205	
Leu Gly Trp Gly Pro Thr Ala Leu Arg Asp Val Pro Phe Ser Ala Leu			
210	215	220	
Tyr Trp Phe Asn Tyr Glu Leu Val Lys Ser Trp Leu Asn Gly Leu Arg			
225	230	235	240
Pro Lys Asp Gln Thr Ser Val Gly Met Ser Phe Val Ala Gly Gly Ile			
245	250	255	
Ser Gly Thr Val Ala Ala Val Leu Thr Leu Pro Phe Asp Val Val Lys			
260	265	270	
Thr Gln Arg Gln Val Ala Leu Gly Ala Met Glu Ala Val Arg Val Asn			
275	280	285	
Pro Leu His Val Asp Ser Thr Trp Leu Leu Leu Arg Arg Ile Arg Ala			
290	295	300	
Glu Ser Gly Thr Lys Gly Leu Phe Ala Gly Phe Leu Pro Arg Ile Ile			
305	310	315	320
Lys Ala Ala Pro Ser Cys Ala Ile Met Ile Ser Thr Tyr Glu Phe Gly			
325	330	335	
Lys Ser Phe Phe Gln Arg Leu Asn Gln Asp Arg Leu Leu Gly Gly			
340	345	350	

&lt;210&gt; 21

&lt;211&gt; 320

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 21

Met Val Gly Tyr Asp Pro Lys Pro Asp Gly Arg Asn Asn Thr Lys Phe			
1	5	10	15
Gln Val Ala Val Ala Gly Ser Val Ser Gly Leu Val Thr Arg Ala Leu			
20	25	30	